REMARKS

The paragraph beginning at page 1, line 2 has been amended to include the number of the U.S. patent issuing from the parent application.

Claims 62 and 98 have been amended for greater clarity without narrowing the scope thereof.

Claim 65 has been amended to incorporate the features of claim 71 and claim 71 has been canceled.

Applicant affirms the election of the claims of Group I for examination in this application. Claims 73-81 have been withdrawn from consideration as being drawn to a non-elected invention.

Upon entry of this amendment, claims 61-70, 72 and 82-104 will be pending in the application.

Claims 61-64, 72 and 82-104

Applicants respectfully request reconsideration of the rejection of claims 61-64, 72, 82-85 and 90-104 under 35 U.S.C. §102(a) as being anticipated by WO 98/07026 A1 (Windhab et al.) and of the rejection of claims 86-89 under 35 U.S.C. §103(a) as being unpatentable over the disclosure in Windhab et al. Applicants submit that the invention defined in these claims is novel and patentable over Windhab.

The present invention is directed to methods for screening members of a combinatorial library (e.g., potential catalysts for a reaction of interest). The method of independent claim 61 is representative and comprises simultaneously flowing a test fluid through six or more vessels, each of which comprises a member of the combinatorial library. The test fluid simultaneously contacts the library members within the vessels. Following contact, changes in the test fluid are simultaneously detected and the changes correlated to a property of each of the library members. In accordance with the present invention, the flowrate of the test fluid is controlled to be about the same in the six or more vessels by simultaneously flowing the test fluid through six or more flow restrictors. The flow restrictors

provide fluid communication between one of the vessels and either an entrance control volume, or alternatively, an exit control volume and can be any passive structure that hinders fluid flow, including capillary tubes and micromachined channels. Importantly, in order to control the flowrate of the test fluid to be about the same in the vessels as claimed, the flow restrictors are designed to exert the greatest resistance to fluid flow along the flow paths between the entrance and exit control volumes. In accordance with claim 63, the fluid flow resistance (i.e., pressure drop) is greatest in the flow restrictors and is approximately the same in each flow restrictor such that the test fluid is apportioned about equally between each of the vessels. This is a significant advantage because the extent of change in the test fluid following contact with a library member depends on, among other things, the time a given amount of test fluid contacts the library member. The catalyst screening variations defined in independent claims 62, 72 and 98 likewise require controlling the flowrate of one or more reactants to be about the same in the reaction vessels by simultaneously flowing the reactants through flow restrictors.

Windhab et al. disclose a process and device for simultaneously investigating potentially catalytic substances in a plurality of miniaturized reactors operated in parallel. The device depicted in Figs. 1 and 2 includes reactors 2 arranged in a square or rectangular pattern in a block-shaped arrangement 3 formed by block 4, spacer plates 9 and 12 and transparent windows 13. The miniature reactors (volume 0.001 to 1 cm^3) and the supply and discharge connections for the supply of liquid and/or gaseous educts to the reactors and the removal of reaction products from the reactors are provided by drillings in the block/plate arrangement. In the disclosed embodiment, the drillings for the reactors are 4 mm, while the drillings 5 for the supply of educt and the drillings 10 for the withdrawal of product are both 2.5 mm. Fluid reactants are introduced through the drillings 5 into contact with the catalyst 8 disposed within the reactors 2 and reaction product mixtures exit the reactors

through drillings 10 into respective cuvette drillings 11 where the mixtures are subjected to spectroscopic analysis (e.g., IR).

The Office action equates the educt supply drillings 5, the cuvette drillings 11 and the reaction mixture withdrawal drillings 10 of the device disclosed by Windhab et al. with the entrance control volume, exit control volume and flow restrictors, respectively, called for in the claimed method. The Office action notes "the small diameter of the microchannel 10 with respect to the reactor diameter 2 ensures the resistance to fluid flow is greater in the flow restrictor." This assertion is unfounded. Specifically, the mere disclosure that the diameter of the purported flow restrictors (i.e., withdrawal drillings 10) is smaller than the diameter of the reactors in Windhab et al.'s device does not mean that the withdrawal drillings necessarily produce a greater resistance to fluid flow than the catalyst bed. Although the calculated area within these two components perpendicular to the direction of fluid flow is approximately 5 and 13 mm^2, respectively, the Office action fails to consider that the **actual** fluid flow area within the reactor is significantly diminished by the presence of the catalyst bed. Accordingly, in the absence of any teaching to the contrary, it is equally likely, if not more likely, that the fluid flow resistance is greatest in the reactors and could vary significantly from one reactor to the next along with the fluid flowrate. In any event, it is not possible to determine, nor is there any suggestion by Windhab et al. that the withdrawal drillings exert the greatest resistance to fluid flow along the flow paths between the supply drillings and the cuvette drillings so as to control the flowrate of the fluid passing through the reactors to be about the same as required in the claimed method.

In view of the above, applicants respectfully submit that the invention defined in independent claims 61, 62, 72 and 98 and claims 63, 64, 82-97, 99-104 depending therefrom is not anticipated nor rendered obvious by the disclosure of Windhab et al.

Claims 65-71

Reconsideration is respectfully requested of the rejection of claims 65, 66, 70 and 71 under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 4,099,923 (Milberger) and of the rejection of claims 67-69 under 35 U.S.C. §103(a) based on the disclosure of Milberger in view of U.S. Patent No. 5,753,185 (Mathews et al.). The invention defined in the pending claims is submitted as both novel and patentable over the disclosure of Milberger and Mathews et al.

The properties of some library members may change during exposure to test fluid. For example, a sample may exhibit high catalytic activity during initial contact with a reactive fluid, but a short time later, may show a precipitous decline in activity. Conversely, a sample may show an increase in catalytic activity with elapsed contact time. In such cases, one must ensure that the time from initial contact with the test fluid to detection of changes in the test fluid is about the same for each sample; otherwise, when using a combination of parallel and serial screening, a sample's perceived performance will depend on position within the screening cycle.

Another method for screening catalysts utilizing the fluid handling system in accordance with the present invention is set forth in independent claim 65. In this method one or more reactants is fed through one or more distribution valves to six or more reaction vessels, each of which comprises an inlet in fluid communication with an entrance control volume, an outlet in fluid communication with an exit control volume, and a different candidate catalyst in the reaction vessel. The distribution valve(s) provides selective fluid communication between the entrance control volume and the reaction vessels. The candidate catalysts are contacted with the reactants in the reaction vessels under reaction conditions for the reaction of interest. Reaction products and any unreacted reactants are discharged from the reaction vessels through one or more selection valves to one or more detectors. The selection valve(s) provides selective

fluid communication between the reaction vessels and the detectors. The contact time for each of the candidate catalysts is controlled to be about the same by synchronized operation of the distribution valve(s) and the selection valve(s). The resulting reaction products or unreacted reactants are detected to determine the efficacy of the six or more catalyst candidates. Claim 65 has been amended to incorporate the requirements of dependent claim 71. As amended, claim 65 further requires that the reactant(s) be fed simultaneously to at least two of the reaction vessels so that the reactant(s) contact at least two of the candidate catalysts simultaneously and reaction products and any unreacted reactants are discharged from the reaction vessels and detected simultaneously (See, for example, the description of the fluid handling system at page 8, line 14 to page 12, line 23; and Example 2 at page 21 of the application).

Milberger discloses an automatic catalyst screening unit including a reactor module 25 defining six reaction chambers for receiving candidate catalysts. In operation, a reactant feeding means 10 selectively feeds the flow of gaseous reactants to each individual reaction chamber in accordance with a predetermined time sequence using a six-way selector valve 27. The gross reaction product passing out of each of the reaction chambers passes through a common outlet manifold 106 and then into an analyzing system 114. A solenoid actuated three-way valve 120 directs the gaseous reaction product to a vent for a reasonable period of time until steady state conditions are reached in a particular vessel and then the valve 120 directs the reaction product into the analyzing system wherein a predetermined volume of gaseous product is transferred to a gas chromatograph 126 for analysis. The selector valve 27 then directs the gaseous reactants to the next in the sequence of reaction chambers and the same procedure is repeated until all six of the catalyst have been tested.

In Milberger, the reactant feed is introduced into each of the reaction chambers and the resulting product analyzed (i.e., detected) individually, in serial fashion. Milberger does

not disclose the requirements of claim 65 of feeding reactants to at least two reaction vessels into simultaneous contact with at least two different candidate catalysts and simultaneously discharging and detecting the resulting reaction products. Further, Milberger does not teach or suggest how one might control the contact time to be about the same for each of the six or more candidate catalysts in a fluid handling system in which reactants simultaneously contact different candidate catalyst in different vessels and the resulting reaction product is simultaneously discharged and detected.

Accordingly, applicants respectfully submit that the invention defined in claim 65 and the claims depending therefrom is not anticipated by Milberger.

The deficiencies of the primary reference with respect to claim 65 cannot be overcome by resort to Mathews et al. Unlike the present invention and the primary reference directed to catalyst screening techniques, Mathews et al. discloses a vehicle emissions testing system to determine the NO_x, CO, CO_2 and uncombusted hydrocarbon content. A conditioned sample of vehicle emissions is introduced into an analyzer 30 wherein the sample is passed through a flow restrictor 40 and split, one portion fed to a reaction cell 60 for chemiluminescence reactions and the other portion fed to a combustion cell 32 for flame ionization analysis.

The testing system disclosed by Mathews et al. does not include multiple vessels containing different catalysts, much less operate by feeding reactants to different catalyst-containing vessels simultaneously and withdrawing and detecting the resulting reaction products simultaneously. Accordingly, the combination of Milberger and Mathews et al. fails to establish a *prima facie* case of obviousness with respect to the invention defined in claim 65. Moreover, although Mathews et al. may mention the use of flow restrictors, the disclosure suggests nothing which would teach or suggests to one skilled in the art the significance of controlling flowrate within multiple vessels

containing candidate catalysts so as to provide meaningful comparative analysis during screening.

In view of the above, applicants respectfully submit that the invention defined in independent claim 65 and claims 66-70 depending therefrom is patentable over Milberger and Mathews et al.

Conclusion

In view of the above, it is respectfully submitted that the pending claims are clearly patentable over the art of record.

Favorable reconsideration and allowance of all pending claims are respectfully solicited.

Applicants request an extension of time to and including May 16, 2003 for filing a response to the above-mentioned Office action. A check in payment of the applicable extension fee is enclosed.

The Commissioner is requested to charge any fee deficiency of overpayment in connection with this amendment to Deposit Account 19-1345.

Respectfully submitted,

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